

# **Introduction to Endocrinology**

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## Topics:

- ⊙ Endocrine vs exocrine gland.
- ⊙ Chemical messengers

## Hormone:

- Definition:
  - Chemical structure.
  - Paracrine, autocrine, endocrine, neuroendocrine.
  - Transport and clearance.
- Mechanism of action:
  - Receptors, down-regulation and up-regulation.
  - Intracellular signaling.
  - Second messenger (cAMP, IP3).

**Guyton and Hall Textbook -  
Medical Physiology- 14th Ed**

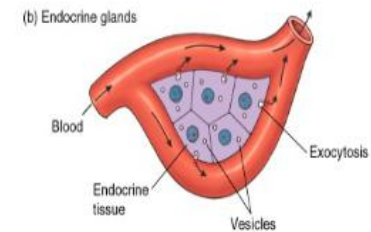
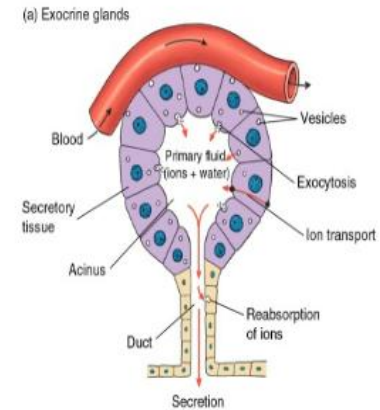
# Glands

## A. Exocrine gland

- Ducts
- Secrets enzymes
- Lumen and surfaces

## B. Endocrine gland

- No ducts
- Secrets Chemical messengers
- Blood stream



# Chemical messengers:

- The activities of cells, tissues and organs are coordinated by chemical messengers:
  - Neurotransmitters
  - Endocrine hormones
  - Neuroendocrine hormones
  - Paracrines
  - Autocrines
  - Cytokines

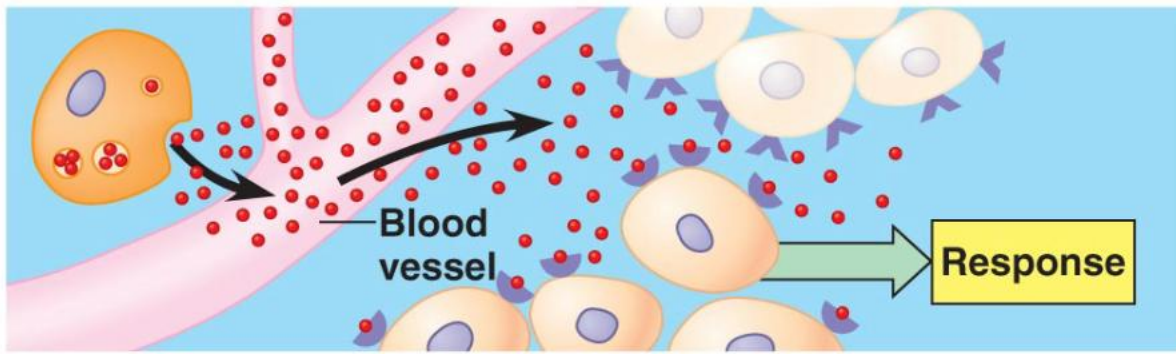


1. **Neurotransmitters** are released by axon terminals of neurons into the synaptic junctions and act locally to control nerve cell functions.
2. **Endocrine hormones** are released by glands or specialized cells into the circulating blood and influence the function of target cells at another location in the body.
3. **Neuroendocrine hormones** are secreted by neurons into the circulating blood and influence the function of target cells at another location in the body.

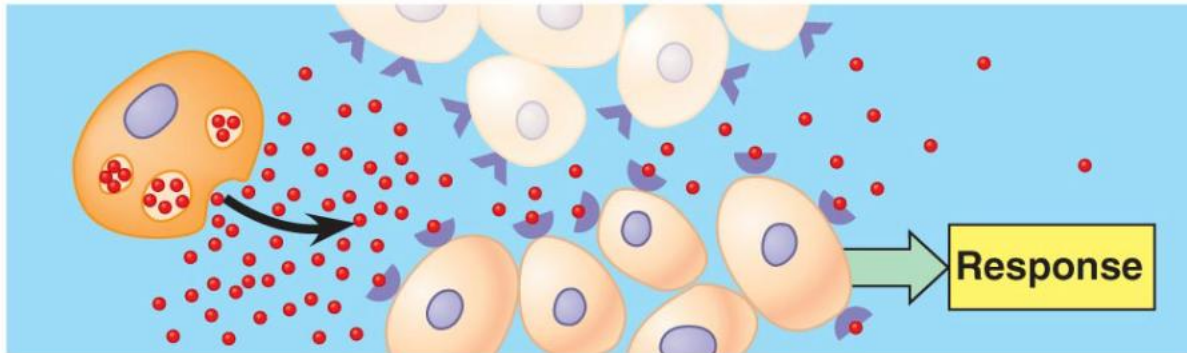
**4. Paracrines** are secreted by cells into the extracellular fluid and affect neighbouring target cells of a different type.

**5. Autocrines** are secreted by cells into the extracellular fluid and affect the function of the same cells that produced them.

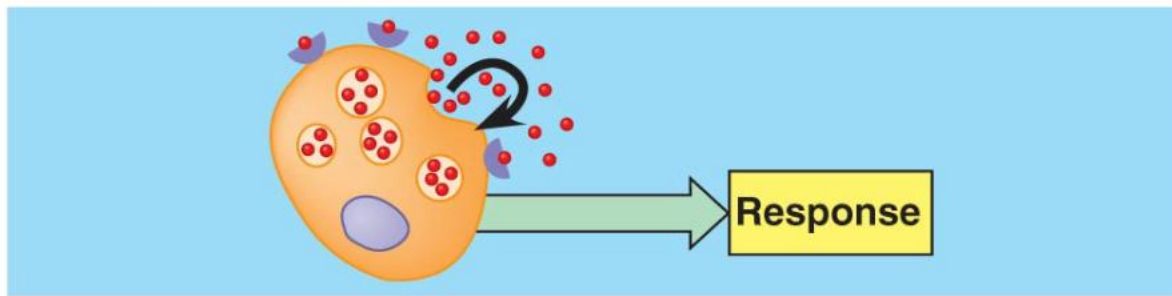
**6. Cytokines** are peptides secreted by cells into the extracellular fluid and can function as autocrines, paracrines, or endocrine hormones. Examples of cytokines include the interleukins.



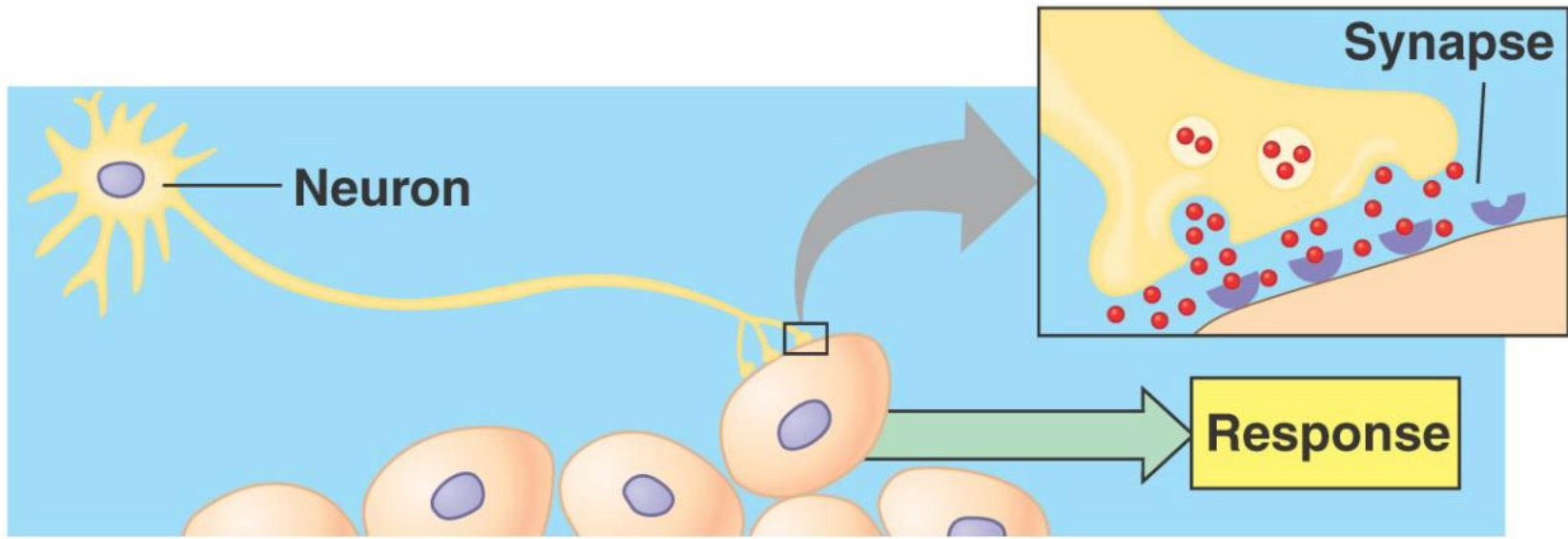
**(a) Endocrine signaling**



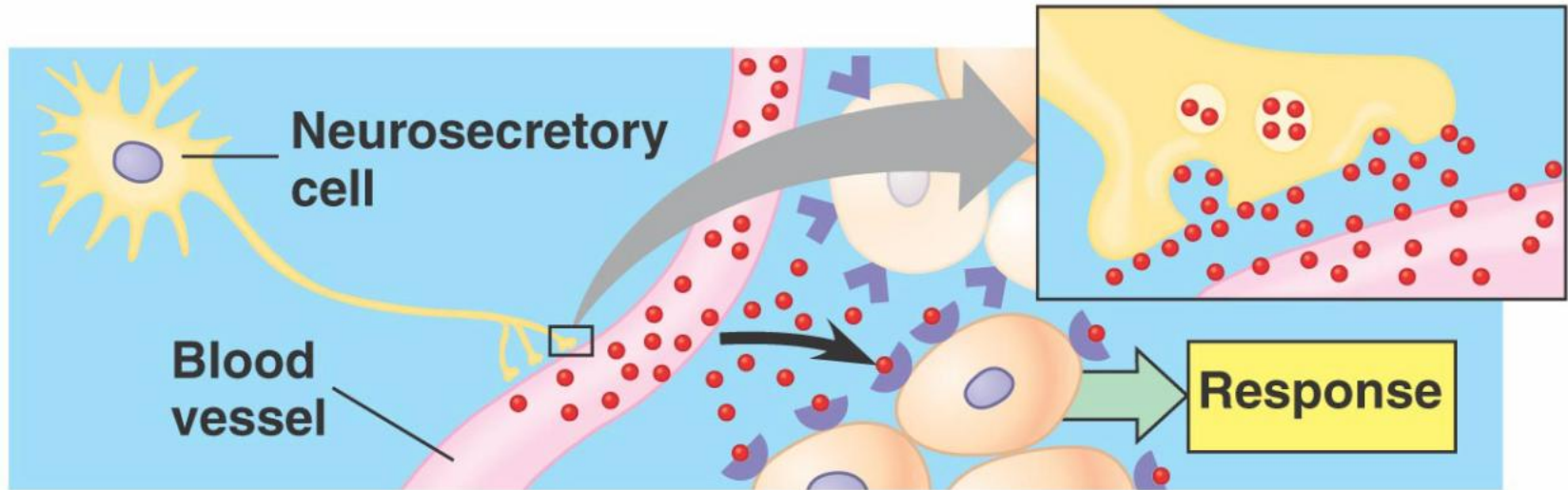
**(b) Paracrine signaling**



**(c) Autocrine signaling**



**(d) Synaptic signaling**



**(e) Neuroendocrine signaling**

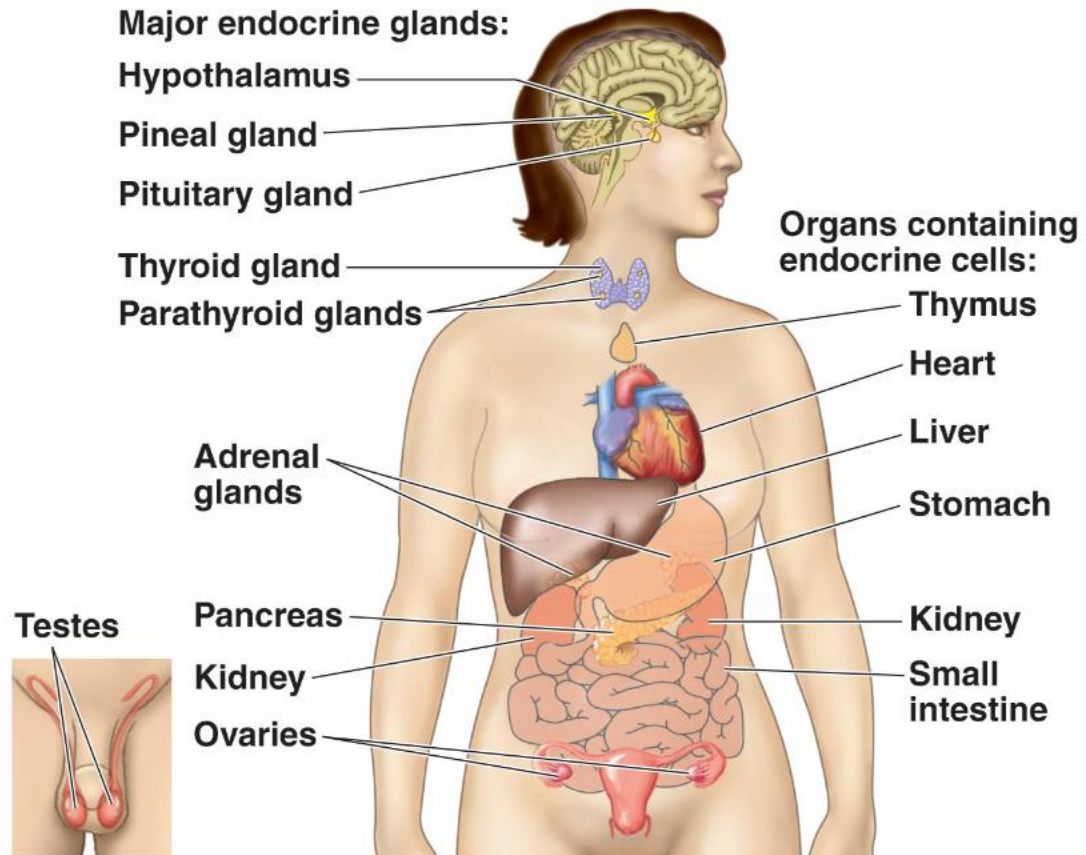
# CYTOKINES

- Peptides (interleukins, lymphokines, adipokines).
- Secreted by cells into extracellular fluid (ECF).
- Can function as endocrine, paracrine or autocrine.

# INTRODUCTION

## ○ Endocrine glands:

- Pituitary
- Thyroid
- Parathyroid
- Adrenal
- Pancreas
- Ovaries
- Testes



- The multiple hormone systems play a key role in regulating almost all body functions:
  - Metabolism
  - Growth and development
  - Water and electrolyte balance
  - Reproduction
  - Behavior

## ⊙ Definition

- ⋮ ■ Hormone is a chemical substance released by group of cells to control the function of other type of cells.

## ⊙ Types of hormones:

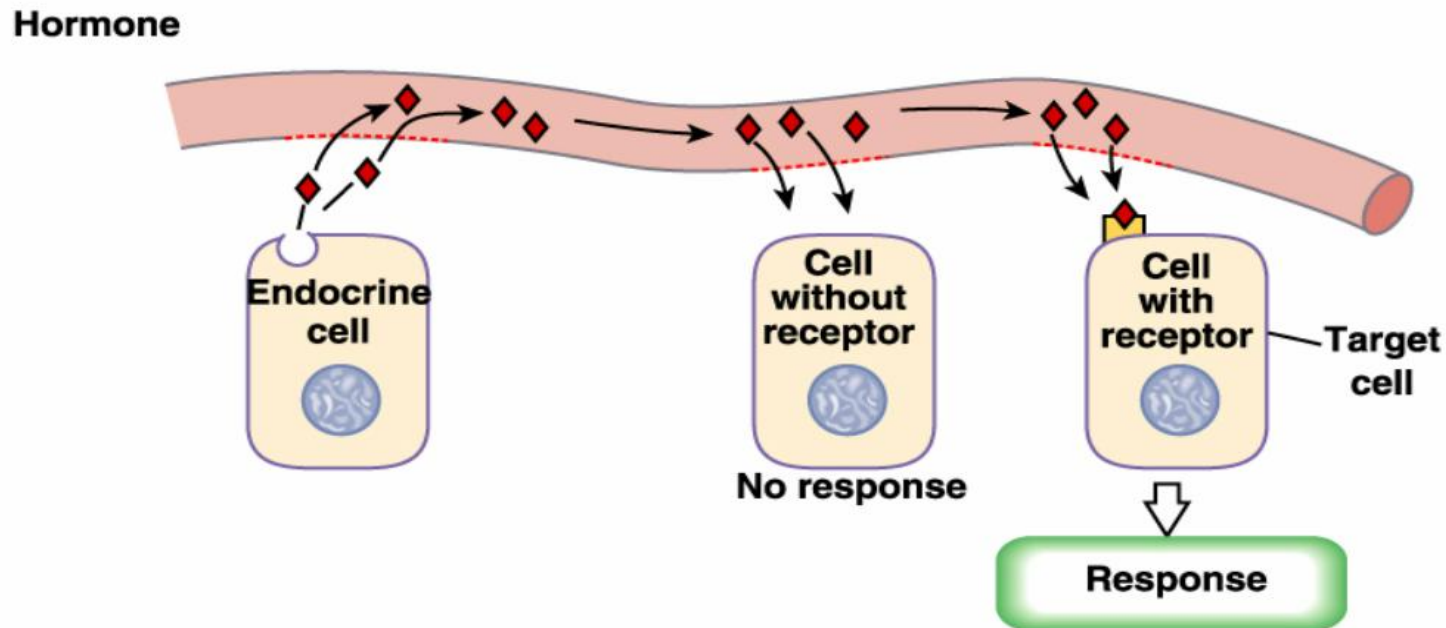
- Affect many different types of cells (eg. GH and Thyroxin).
- Affect only specific target cells (eg. ACTH and estrogen).



# INTRODUCTION

- What are **target cells**?

Target cells refer to cells that contain specific receptors (binding sites) for a particular hormone.



# ❖ Chemical Structure and Synthesis of Hormones

There are *3 general classes* of hormones

## **1- Proteins and polypeptides:** [stored in vesicles until needed]

- anterior and posterior pituitary gland
- pancreas (insulin and glucagon)
- parathyroid gland (parathyroid hormone)

## **2- Steroids:** [diffuse across the cell membrane]

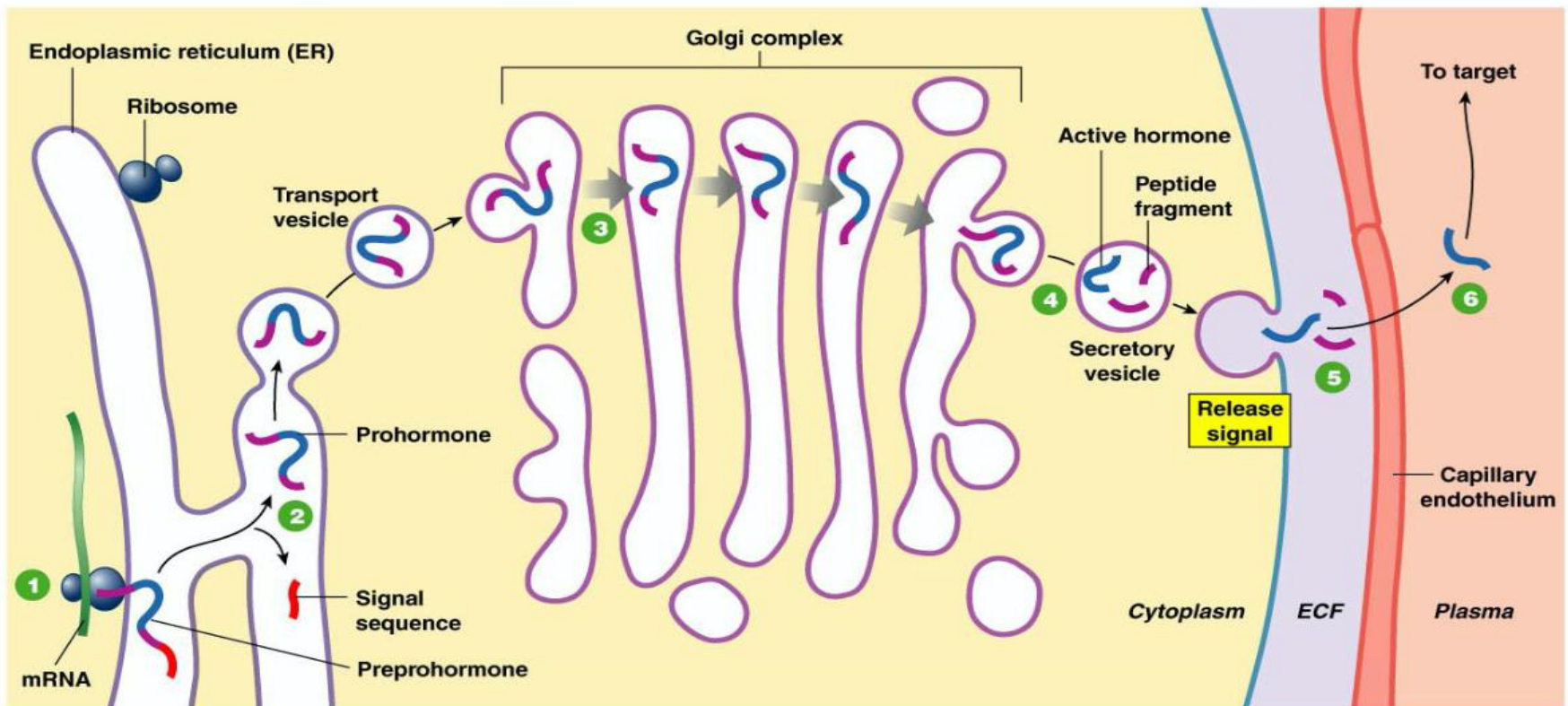
- adrenal cortex (cortisol and aldosterone)
- ovaries (estrogen and progesterone)
- testes (testosterone)

## **3- Derivatives of the amino acid tyrosine:**

- thyroid hormones.
- adrenal medullae (epinephrine and norepinephrine)

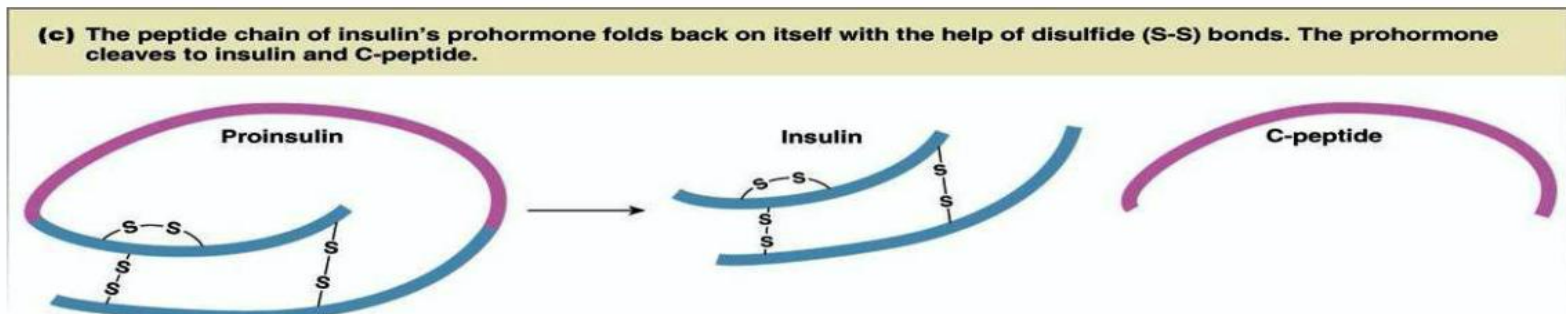
# PEPTIDE (PROTEIN) HORMONES

- Synthesized as **preprohormone** → **post-translational modification** to **prohormone** → then **hormone**



# PEPTIDE (PROTEIN) HORMONES

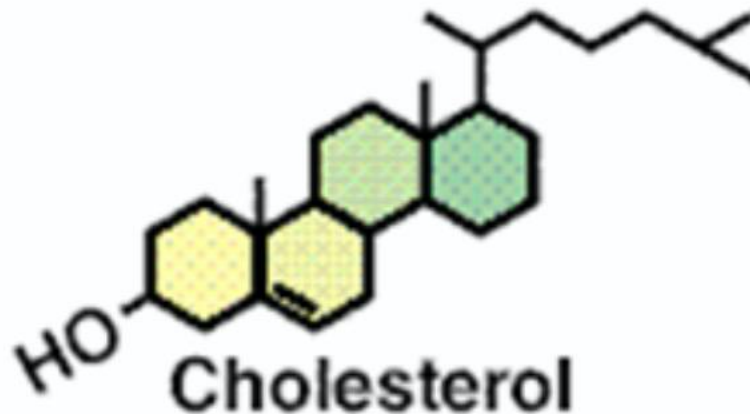
- Example of protein hormone:
  - Insulin



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# STEROID HORMONES

- Secreted by gonads, adrenals, placenta.
- Derived from cholesterol (lipophilic)
  - Cross membranes (no storage)
- On-demand synthesis (SER)
- Usually Bound to **Carrier** proteins



# AMINE HORMONES

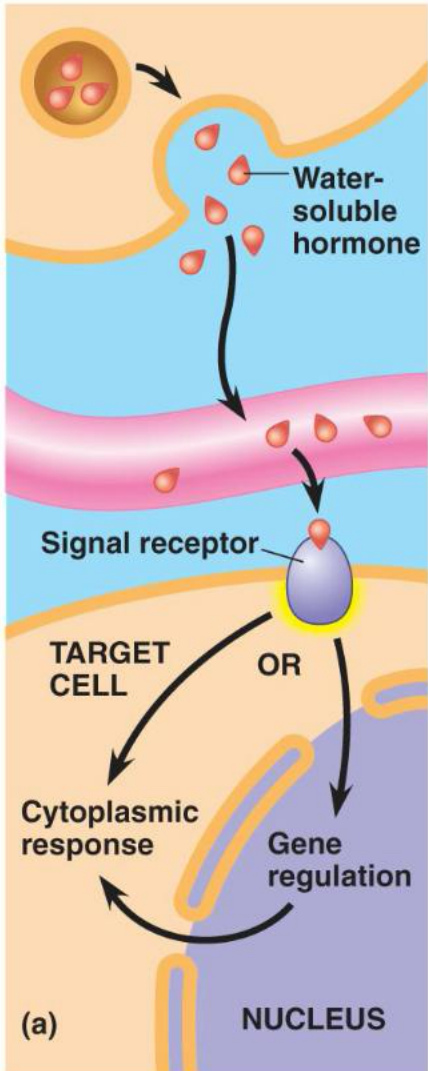
- ◉ Derived from tyrosine or tryptophan.
- ◉ 3 groups
  - Tryptophan  $\Rightarrow$  Melatonin
  - Tyrosine  $\Rightarrow$  Catecholamines  
behave like peptide hormones
  - Tyrosine  $\Rightarrow$  Thyroid hormones  
behave like steroid hormones

# TRANSPORT OF HORMONES

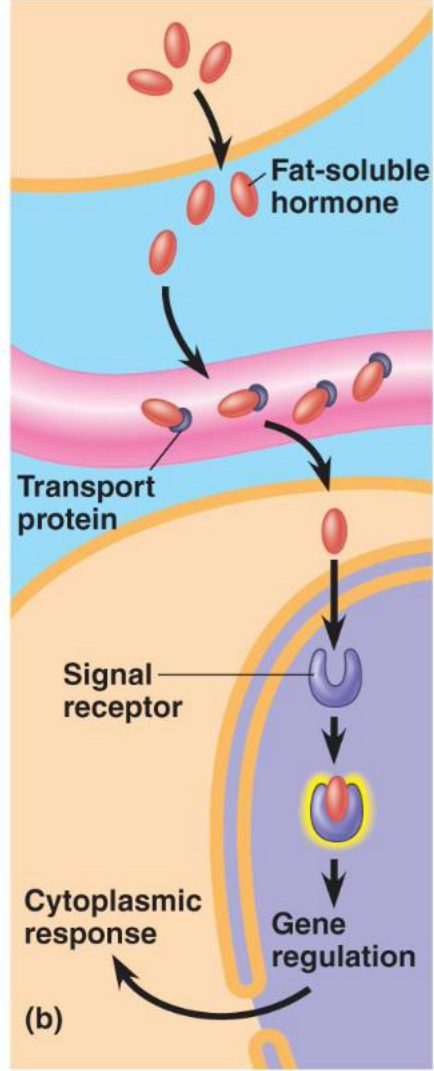
- Water soluble hormones- hydrophilic (peptides & catecholamines) dissolved in Plasma.
- Fat soluble hormones - hydrophobic Steroids and thyroid hormones transported bound to plasma proteins (90%),  
binding to proteins helps to:
  - Provide reservoirs.
  - Slow hormones clearance.



# The differences between water-soluble & fat-soluble hormones



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# HORMONES & RECEPTORS

## ○ Receptors:

- Hormonal receptors are large proteins.
- 2000-100,000 receptors/cell.
- Receptors are highly specific for a single hormone.

## ○ Receptor's Location:

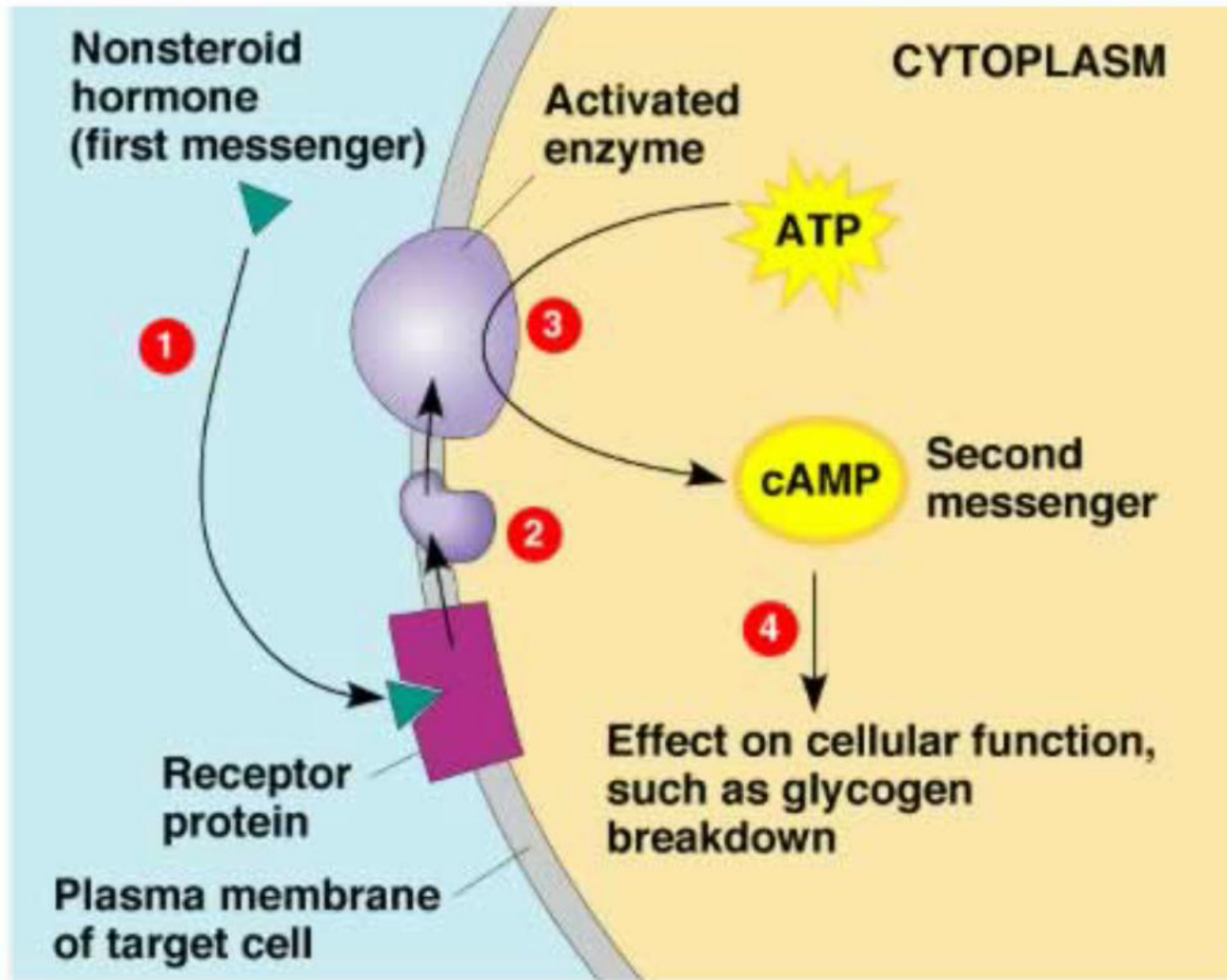
- On the surface of cell membrane (proteins, peptides and catecholamines).
- In the cell cytoplasm (Steroids).
- In the cell nucleus (thyroid hormones).

# MECHANISM OF ACTION OF HORMONES

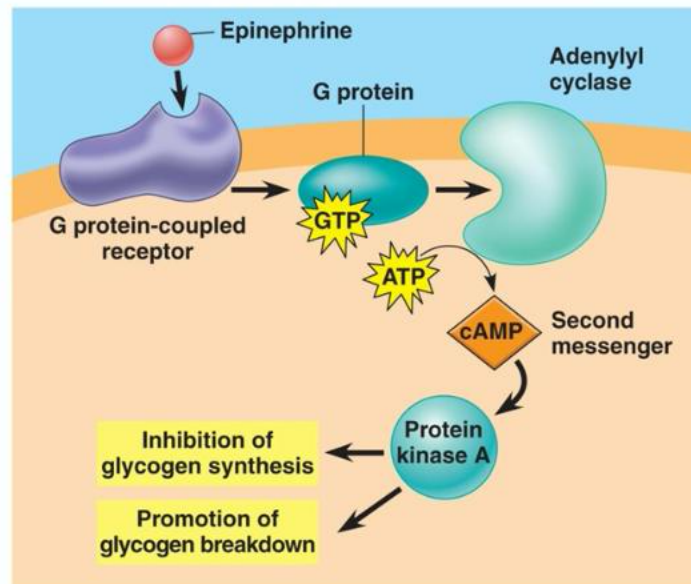
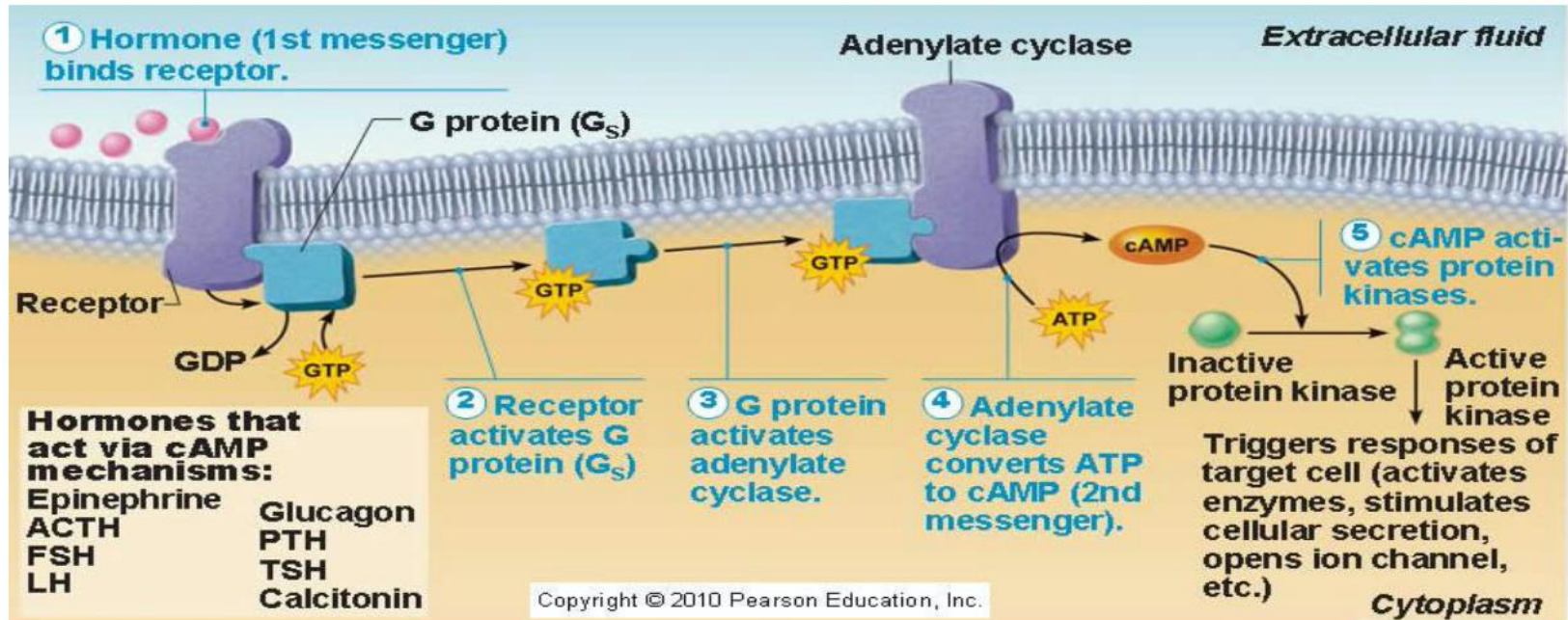
## ○ Mechanism of action:

1. Hormone-receptor interaction (1<sup>st</sup> messenger)
2. Enzyme activation.
3. Release of the second messenger.
4. Effects on cellular function.

# MECHANISM OF ACTION (PEPTIDES AND PROTEIN HORMONES)

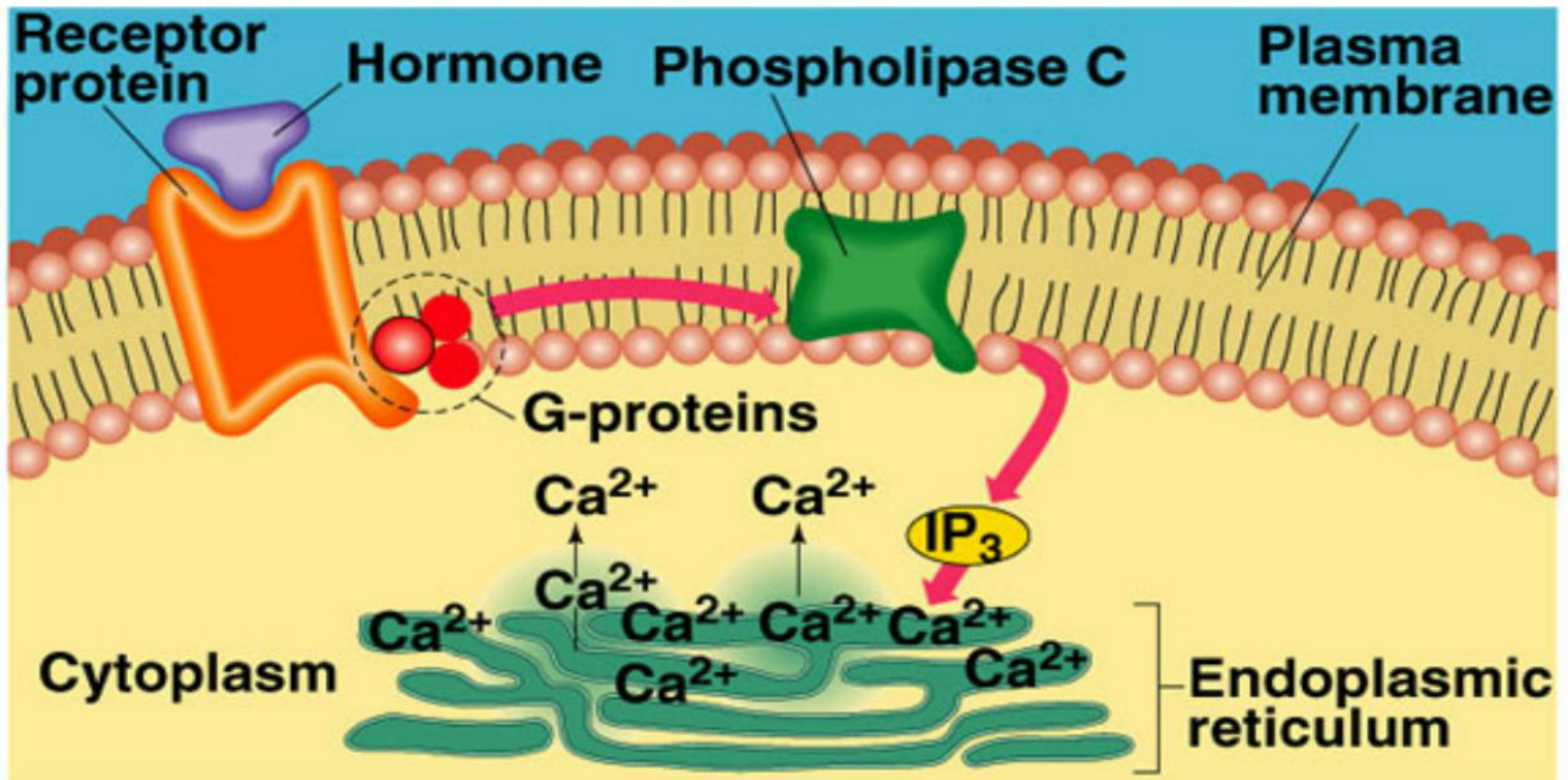


# SECOND MESSENGER (ADENYLYLATE CYCLASE-CAMP)

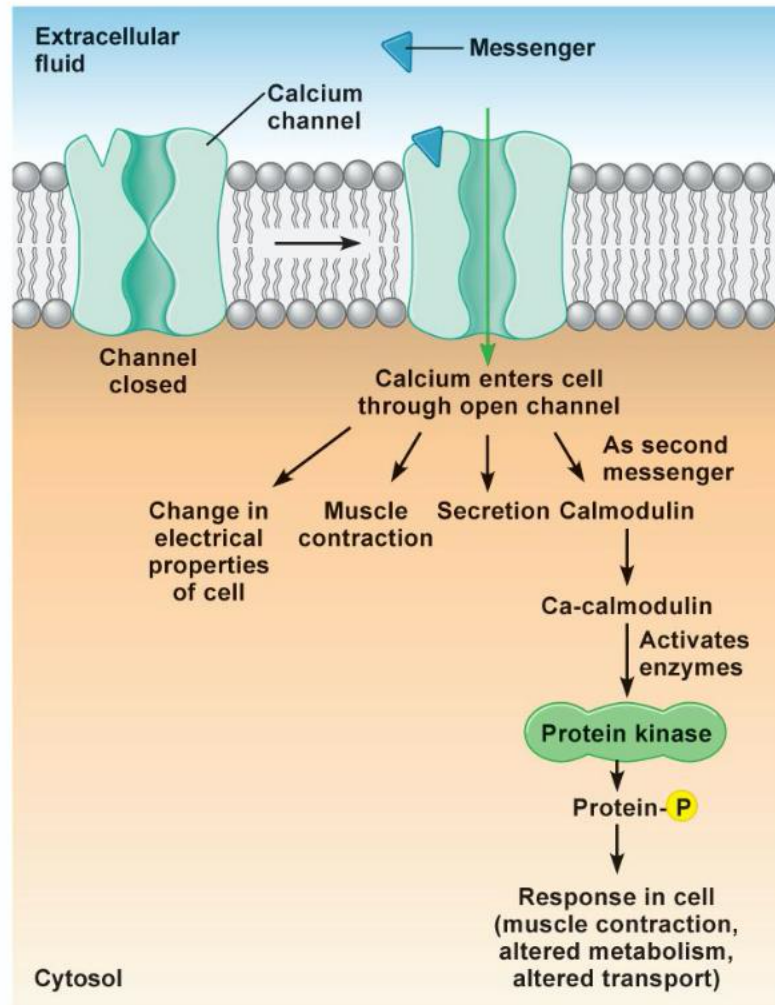




# SECOND MESSENGER (PHOSPHOLIPASE C-IP<sub>3</sub>)

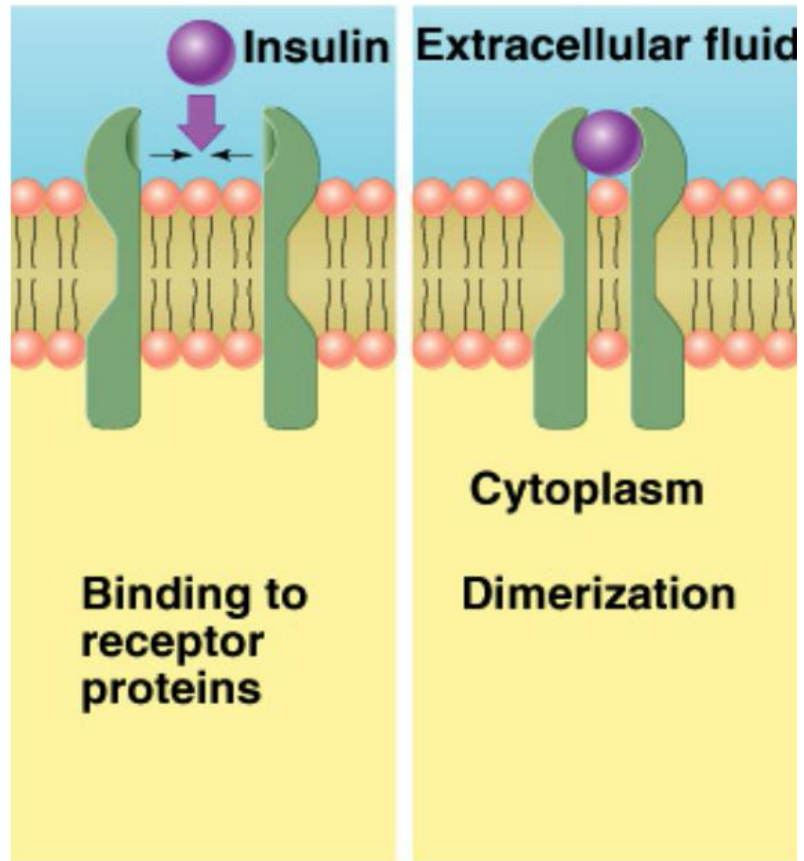


# SECOND MESSENGER (CALCIUM-CALMODULIN COMPLEX)



# SECOND MESSENGER (TYROSINE KINASE SYSTEM)

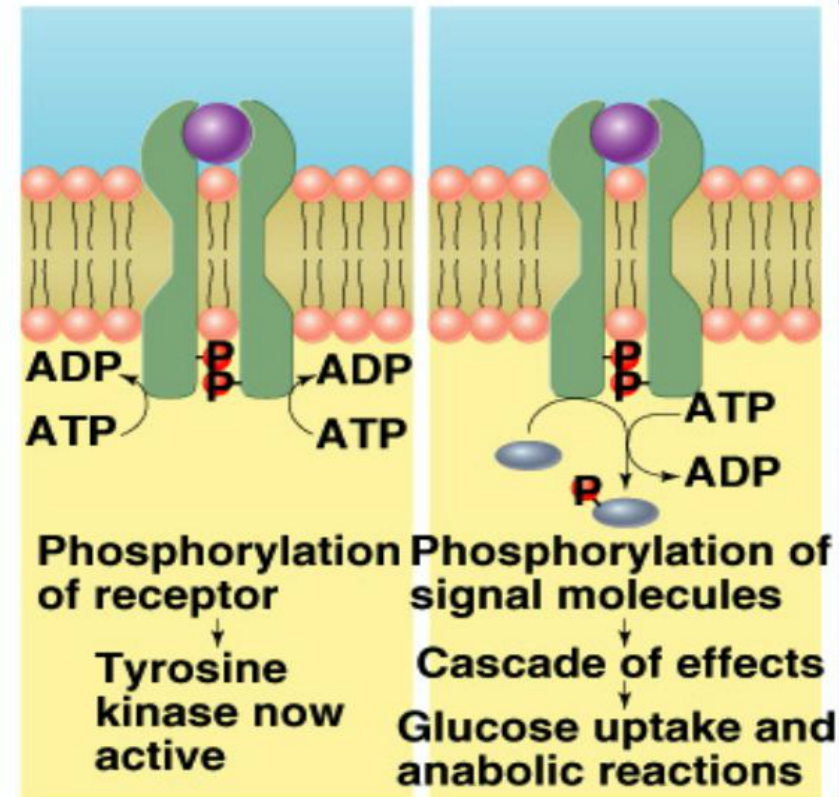
- Is used by insulin & many growth factors to cause cellular effects.
- Surface receptor is tyrosine kinase
  - Consists of 2 units that form active dimer when insulin binds.





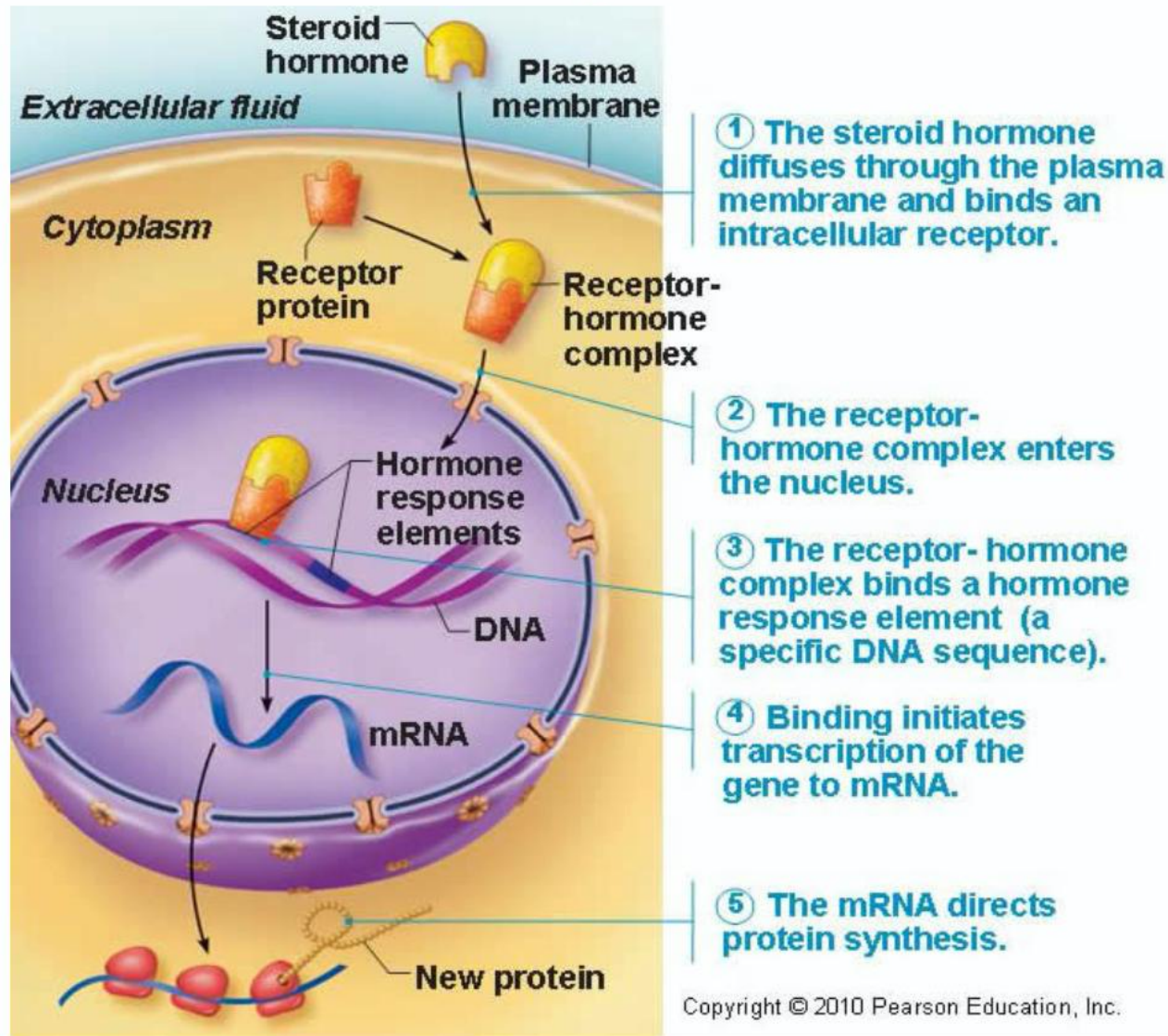
# SECOND MESSENGER (TYROSINE KINASE SYSTEM)

- Activated tyrosine kinase phosphorylates signalling molecules.
- Induction of hormone/growth factor effects.





# MECHANISM OF ACTION (STEROID HORMONES)



# REGULATION OF HORMONAL RECEPTORS

- Receptors does not remain constant
    - Inactivated or destroyed
    - Reactivated or manufactured
  - **Downregulation**
    - Increase hormone concentration leads to decrease in the number of active receptors.
    - Most peptide hormones have pulsatile secretion which prevents downregulation.
  - **Upregulation**
    - The hormone induces greater than normal formation of a receptor or intracellular signaling proteins.
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# CLEARANCE OF HORMONES

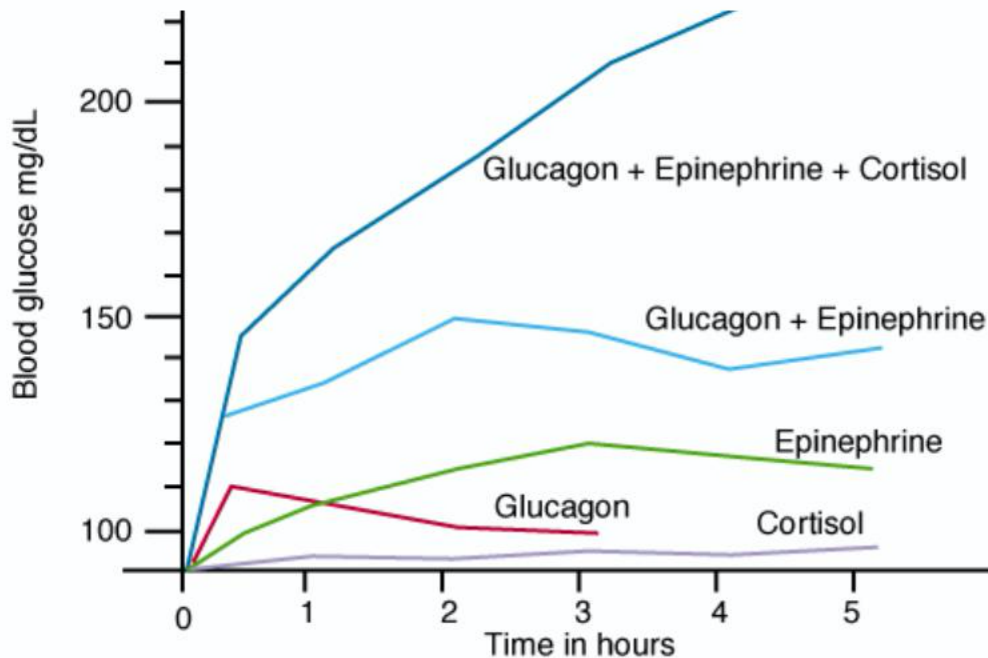
- Two factors control the concentration of a hormone in the blood:
  - The rate of its secretion
  - The rate of its removal (metabolic clearance)
- Hormones are cleared by:
  - Metabolic destruction by tissues
  - Binding with tissues
  - Excretion by the liver into bile
  - Excretion by the kidney into urine
- Clearance of protein bound hormones is slower than clearance of peptide hormones

# HORMONE INTERACTIONS

- Multiple hormones can affect a single target simultaneously
- Three types of hormone interactions:
  1. Synergism
  2. Permissiveness
  3. Antagonism

# SYNERGISM

- ◉ Combined action of hormones is more than just additive.
- ◉ Example: Blood glucose levels & synergistic effects of glucagon, cortisol and epinephrine.



# PERMISSIVENESS

- **One hormone allows another hormone to have its full effect**
  - Especially during growth.
- **Example**
  - Thyroid hormone have permissive effect on growth hormone action.
  - Deficiency of thyroid hormone in infants leads to dwarfism.

# ANTAGONISM

- Antagonistic hormones have opposing physiological actions.
  - Hormone B diminishes the effect of hormone A
- Example
  - Glucagon antagonizes the action of insulin.

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